



7/4

SEQUENCE LISTING

<100> Freckling, Terry M.
<100> Shatyev, George M.

<120> COMPOSITIONS AND METHODS FOR TREATING HEMORRHAGIC VIRUS
INFECTIONS AND OTHER DISORDERS

<130> 24881-301D

<140> US/10/038,557

<141> 2002-01-03

<150> 09/840,707

<151> 2001-04-23

<150> 09/562,979

<151> 2000-04-27

<150> 60/198,210

<151> 1999-04-27

<160> 26

<170> PatentIn Ver. 2.0

<210> 1

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<212> PRT

<213> Homo sapiens

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<223> Recombinant Interleukin 1-alpha

<300>

<308> AAA59134/GenBank

<309> 1994-12-13

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Lys Ser Phe Tyr His Val Ser Tyr Gly Pro Leu His Glu Gly Cys Met
35 40 45
Asp Gln Ser Val Ser Leu Ser Ile Ser Glu Thr Ser Lys Thr Ser Lys
50 55 60
Leu Thr Phe Lys Glu Ser Met Val Val Val Ala Thr Asn Gly Lys Val
65 70 75 80
Leu Lys Lys Arg Arg Leu Ser Leu Ser Gln Ser Ile Thr Asp Asp Asp
85 90 95
Leu Glu Ala Ile Ala Asn Asp Ser Glu Glu Glu Ile Ile Lys Pro Arg
100 105 110
Ser Ala Pro Phe Ser Phe Leu Ser Asn Val Lys Tyr Asn Phe Met Arg
115 120 125
Ile Ile Lys Tyr Glu Phe Ile Leu Asn Asp Ala Leu Asn Gln Ser Ile
130 135 140
Ile Arg Ala Asn Asp Gln Tyr Leu Thr Ala Ala Ala Leu His Asn Leu

145 150 155 160
 Asp Glu Ala Val Lys Phe Asp Met Gly Ala Tyr Lys Ser Ser Lys Asp
 165 170 175
 Asp Ala Lys Ile Thr Val Ile Leu Arg Ile Ser Lys Thr Gln Leu Tyr
 180 185 190
 Val Thr Ala Gln Asp Glu Asp Gln Pro Val Leu Leu Lys Glu Met Pro
 195 200 205
 Glu Ile Pro Lys Thr Ile Thr Gly Ser Glu Thr Asn Leu Leu Phe Phe
 210 215 220
 Trp Glu Thr His Gly Thr Lys Asn Tyr Phe Thr Ser Val Ala His Pro
 225 230 235 240
 Asn Leu Phe Ile Ala Thr Lys Gln Asp Tyr Trp Val Cys Leu Ala Gly
 245 250 255
 Gly Pro Pro Ser Ile Thr Asp Phe Gln Ile Leu Glu Asn Gln Ala
 260 265 270

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 <300>
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 <309> 1986-07-21

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 Lys Cys Ser Phe Gln Asp Leu Asp Leu Cys Pro Leu Asp Gly Gly Ile
 35 40 45
 Gln Leu Arg Ile Ser Asp His His Tyr Ser Lys Gly Phe Arg Gln Ala
 50 55 60
 Ala Ser Val Val Val Ala Met Asp Lys Leu Arg Lys Met Leu Val Pro
 65 70 75 80
 Cys Pro Gln Thr Phe Gln Glu Asn Asp Leu Ser Thr Phe Phe Pro Phe
 85 90 95
 Ile Phe Glu Glu Glu Pro Ile Phe Phe Asp Thr Trp Asp Asn Glu Ala
 100 105 110
 Tyr Val His Asp Ala Pro Val Arg Ser Leu Asn Cys Thr Leu Arg Asp
 115 120 125
 Ser Gln Gln Lys Ser Leu Val Met Ser Gly Pro Tyr Glu Leu Lys Ala
 130 135 140
 Leu His Leu Gln Gly Gln Asp Met Glu Gln Gln Val Val Phe Ser Met

145		150		155		160
Ser Phe Val Gln Gly Glu Glu Ser Asn Asp Lys Ile Pro Val Ala Leu	165	170	175			
Gly Leu Lys Glu Lys Asn Leu Tyr Leu Ser Cys Val Leu Lys Asp Asp	180	185	190			
Lys Pro Thr Leu Gln Leu Glu Ser Val Asp Pro Lys Asn Tyr Pro Lys	195	200	205			
Lys Lys Met Glu Lys Arg Phe Val Phe Asn Lys Ile Glu Ile Asn Asn	210	215	220			
Lys Leu Glu Phe Glu Ser Ala Gln Phe Pro Asn Trp Tyr Ile Ser Thr	225	230	235			240
Ser Gln Ala Glu Asn Met Pro Val Phe Leu Gly Gly Thr Lys Gly Gly	245	250	255			
Gln Asp Ile Thr Asp Phe Thr Met Gln Phe Val Ser Ser	260	265				

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 <223> Interleukin-1 receptor, Type I precursor

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 <309> 1990-04-01

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Met Lys Val Leu Leu Arg Leu Ile Cys Phe Ile Ala Leu Leu Ile Ser	1 5 10 15
Ser Leu Glu Ala Asp Lys Cys Lys Glu Arg Glu Glu Lys Ile Ile Leu	20 25 30
Val Ser Ser Ala Asn Glu Ile Asp Val Arg Pro Cys Pro Leu Asn Pro	35 40 45
Asn Glu His Lys Gly Thr Ile Thr Trp Tyr Lys Asp Asp Ser Lys Thr	50 55 60
Pro Val Ser Thr Glu Gln Ala Ser Arg Ile His Gln His Lys Glu Lys	65 70 75 80
Leu Trp Phe Val Pro Ala Lys Val Glu Asp Ser Gly His Tyr Tyr Cys	85 90 95
Val Val Arg Asn Ser Ser Tyr Cys Leu Arg Ile Lys Ile Ser Ala Lys	100 105 110
Phe Val Glu Asn Glu Pro Asn Leu Cys Tyr Asn Ala Gln Ala Ile Phe	115 120 125
Lys Gln Lys Leu Pro Val Ala Gly Asp Gly Gly Leu Val Cys Pro Tyr	130 135 140
Met Glu Phe Phe Lys Asn Glu Asn Asn Glu Leu Pro Lys Leu Gln Trp	

145					150					155					160
Tyr	Lys	Asp	Cys	Lys	Pro	Leu	Leu	Leu	Asp	Asn	Ile	His	Phe	Ser	Gly
				165					170					175	
Val	Lys	Asp	Arg	Leu	Ile	Val	Met	Asn	Val	Ala	Glu	Lys	His	Arg	Gly
			180					185					190		
Asn	Tyr	Thr	Cys	His	Ala	Ser	Tyr	Thr	Tyr	Leu	Gly	Lys	Gln	Tyr	Pro
		195					200					205			
Ile	Thr	Arg	Val	Ile	Glu	Phe	Ile	Thr	Leu	Glu	Glu	Asn	Lys	Pro	Thr
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Arg	Pro	Val	Ile	Val	Ser	Pro	Ala	Asn	Glu	Thr	Met	Glu	Val	Asp	Leu
225					230					235					240
Gly	Ser	Gln	Ile	Gln	Leu	Ile	Cys	Asn	Val	Thr	Gly	Gln	Leu	Ser	Asp
				245					250					255	
Ile	Ala	Tyr	Trp	Lys	Trp	Asn	Gly	Ser	Val	Ile	Asp	Glu	Asp	Asp	Pro
			260					265					270		
Val	Leu	Gly	Glu	Asp	Tyr	Tyr	Ser	Val	Glu	Asn	Pro	Ala	Asn	Lys	Arg
		275					280					285			
Arg	Ser	Thr	Leu	Ile	Thr	Val	Leu	Asn	Ile	Ser	Glu	Ile	Glu	Ser	Arg
	290					295					300				
Phe	Tyr	Lys	His	Pro	Phe	Thr	Cys	Phe	Ala	Lys	Asn	Thr	His	Gly	Ile
305					310					315					320
Asp	Ala	Ala	Tyr	Ile	Gln	Leu	Ile	Tyr	Pro	Val	Thr	Asn	Phe	Gln	Lys
				325					330					335	
His	Met	Ile	Gly	Ile	Cys	Val	Thr	Leu	Thr	Val	Ile	Ile	Val	Cys	Ser
			340					345					350		
Val	Phe	Ile	Tyr	Lys	Ile	Phe	Lys	Ile	Asp	Ile	Val	Leu	Trp	Tyr	Arg
		355					360					365			
Asp	Ser	Cys	Tyr	Asp	Phe	Leu	Pro	Ile	Lys	Ala	Ser	Asp	Gly	Lys	Thr
	370					375					380				
Tyr	Asp	Ala	Tyr	Ile	Leu	Tyr	Pro	Lys	Thr	Val	Gly	Glu	Gly	Ser	Thr
385					390					395					400
Ser	Asp	Cys	Asp	Ile	Phe	Val	Phe	Lys	Val	Leu	Pro	Glu	Val	Leu	Glu
				405					410					415	
Lys	Gln	Cys	Gly	Tyr	Lys	Leu	Phe	Ile	Tyr	Gly	Arg	Asp	Asp	Tyr	Val
			420					425					430		
Gly	Glu	Asp	Ile	Val	Glu	Val	Ile	Asn	Glu	Asn	Val	Lys	Lys	Ser	Arg
		435					440					445			
Arg	Leu	Ile	Ile	Ile	Leu	Val	Arg	Glu	Thr	Ser	Gly	Phe	Ser	Trp	Leu
	450					455					460				
Gly	Gly	Ser	Ser	Glu	Glu	Gln	Ile	Ala	Met	Tyr	Asn	Ala	Leu	Val	Gln
465					470					475					480
Asp	Gly	Ile	Lys	Val	Val	Leu	Leu	Glu	Leu	Glu	Lys	Ile	Gln	Asp	Tyr
				485					490					495	
Glu	Lys	Met	Pro	Glu	Ser	Ile	Lys	Phe	Ile	Lys	Gln	Lys	His	Gly	Ala

500 505 510
 Ile Arg Trp Ser Gly Asp Phe Thr Gln Gly Pro Gln Ser Ala Lys Thr
 515 520 525
 Arg Phe Trp Lys Asn Val Arg Tyr His Met Pro Val Gln Arg Arg Ser
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 545 550 555 560
 Gln Arg Glu Ala His Val Pro Leu Gly
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 <308> P27930/GenBank
 <309> 1993-08-01

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 Arg His Tyr Lys Arg Glu Phe Arg Leu Glu Gly Glu Pro Val Ala Leu
 35 40 45
 Arg Cys Pro Gln Val Pro Tyr Trp Leu Trp Ala Ser Val Ser Pro Arg
 50 55 60
 Ile Asn Leu Thr Trp His Lys Asn Asp Ser Ala Arg Thr Val Pro Gly
 65 70 75 80
 Glu Glu Glu Thr Arg Met Trp Ala Gln Asp Gly Ala Leu Trp Leu Leu
 85 90 95
 Pro Ala Leu Gln Glu Asp Ser Gly Thr Tyr Val Cys Thr Thr Arg Asn
 100 105 110
 Ala Ser Tyr Cys Asp Lys Met Ser Ile Glu Leu Arg Val Phe Glu Asn
 115 120 125
 Thr Asp Ala Phe Leu Pro Phe Ile Ser Tyr Pro Gln Ile Leu Thr Leu
 130 135 140
 Ser Thr Ser Gly Val Leu Val Cys Pro Asp Leu Ser Glu Phe Thr Arg
 145 150 155 160
 Asp Lys Thr Asp Val Lys Ile Gln Trp Tyr Lys Asp Ser Leu Leu Leu
 165 170 175
 Asp Lys Asp Asn Glu Lys Phe Leu Ser Val Arg Gly Thr Thr His Leu
 180 185 190
 Leu Val His Asp Val Ala Leu Glu Asp Ala Gly Tyr Tyr Arg Cys Val
 195 200 205
 Leu Thr Phe Ala His Glu Gly Gln Gln Tyr Asn Ile Thr Arg Ser Ile

210		215		220
Glu Leu Arg Ile Lys	Lys Lys Lys Glu Glu Thr	Ile Pro Val Ile Ile		
225	230	235	240	
Ser Pro Leu Lys Thr	Ile Ser Ala Ser Leu Gly	Ser Arg Leu Thr Ile		
	245	250	255	
Pro Cys Lys Val Phe	Leu Gly Thr Gly Thr	Pro Leu Thr Thr Met Leu		
	260	265	270	
Trp Trp Thr Ala Asn	Asp Thr His Ile Glu Ser	Ala Tyr Pro Gly Gly		
	275	280	285	
Arg Val Thr Glu Gly	Pro Arg Gln Glu Tyr Ser	Glu Asn Asn Glu Asn		
	290	295	300	
Tyr Ile Glu Val Pro	Leu Ile Phe Asp Pro Val	Thr Arg Glu Asp Leu		
305	310	315	320	
His Met Asp Phe Lys	Cys Val Val His Asn Thr	Leu Ser Phe Gln Thr		
	325	330	335	
Leu Arg Thr Thr Val	Lys Glu Ala Ser Ser Thr	Phe Ser Trp Gly Ile		
	340	345	350	
Val Leu Ala Pro Leu	Ser Leu Ala Phe Leu Val	Leu Gly Gly Ile Trp		
	355	360	365	
Met His Arg Arg Cys	Lys His Arg Thr Gly Lys	Ala Asp Gly Leu Thr		
	370	375	380	
Val Leu Trp Pro His	His Gln Asp Phe Gln Ser	Tyr Pro Lys		
385	390	395		

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 Precursor (IL-1RA; ICIL-1RA; IRAP)

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 <309> 1990-11-01

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20 25 30
Ser Lys Met Gln Ala Phe Arg Ile Trp Asp Val Asn Gln Lys Thr Phe
35 40 45
Tyr Leu Arg Asn Asn Gln Leu Val Ala Gly Tyr Leu Gln Gly Pro Asn
50 55 60
Val Asn Leu Glu Glu Lys Ile Asp Val Val Pro Ile Glu Pro His Ala
65 70 75 80
Leu Phe Leu Gly Ile His Gly Gly Lys Met Cys Leu Ser Cys Val Lys

	85		90		95
Ser Gly Asp Glu Thr Arg Leu Gln Leu Glu Ala Val Asn Ile Thr Asp	100		105		110
Leu Ser Glu Asn Arg Lys Gln Asp Lys Arg Phe Ala Phe Ile Arg Ser	115		120		125
Asp Ser Gly Pro Thr Thr Ser Phe Glu Ser Ala Ala Cys Pro Gly Trp	130		135		140
Phe Leu Cys Thr Ala Met Glu Ala Asp Gln Pro Val Ser Leu Thr Asn	145		150		155
Met Pro Asp Glu Gly Val Met Val Thr Lys Phe Tyr Phe Gln Glu Asp	165		170		175

Glu

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<223> IL-1 receptor intracellular ligand protein
comprising amino acid sequence

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<310> 5,817,476

<311> 1995-06-07

<312> 1998-10-06

<400> 6

Ile Pro Arg Val Asp Leu Arg Val Trp Gln Asp Cys Cys Glu Asp Cys	1	5	10	15
Arg Thr Arg Gly Gln Phe Asn Ala Phe Ser Tyr His Phe Arg Gly Arg	20	25	30	
Arg Ser Leu Glu Phe Ser Tyr Gln Glu Asp Lys Pro Thr Lys Lys Thr	35	40	45	
Arg Pro Arg Lys Ile Pro Ser Val Gly Arg Gln Gly Glu His Leu Ser	50	55	60	
Asn Ser Thr Ser Ala Phe Ser Thr Arg Ser Asp Ala Ser Gly Thr Asn	65	70	75	80
Asp Phe Arg Glu Phe Val Leu Glu Met Gln Lys Thr Ile Thr Asp Leu	85	90	95	
Arg Thr Gln Ile Lys Lys Leu Glu Ser Arg Leu Ser Thr Thr Glu Cys	100	105	110	
Val Asp Ala Gly Gly Glu Ser His Ala Asn Asn Thr Lys Trp Lys Lys	115	120	125	
Asp Ala Cys Thr Ile Cys Glu Cys Lys Asp Gly Gln Val Thr Cys Phe	130	135	140	
Val Glu Ala Cys Pro Pro Ala Thr Cys Ala Val Pro Val Asn Ile Pro	145	150	155	160
Gly Ala Cys Cys Pro Val Cys Leu Gln Lys Arg Ala Glu Glu Lys Pro				

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 comprising amino acid sequence

<300>
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 <311> 1995-06-07
 <312> 1998-10-06

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 20 25 30
 Ser Phe Glu Gly Lys Arg Arg Leu Leu Ile Thr Ala Pro Lys Ala
 35 40 45
 Glu Asn Asn Met Tyr Val Gln Gln Arg Asp Glu Tyr Leu Glu Ser Phe
 50 55 60
 Cys Lys Met Ala Thr Arg Lys Ile Ser Val Ile Thr Ile Phe Gly Pro
 65 70 75 80
 Val Asn Asn Ser Thr Met Lys Ile Asp His Phe Gln Leu Asp Asn Glu
 85 90 95
 Lys Pro Met Arg Val Val Asp Asp Glu Asp Leu Val Asp Gln Arg Leu
 100 105 110
 Ile Ser Glu Leu Arg Lys Glu Tyr Gly Met Thr Tyr Asn Asp Phe Phe
 115 120 125
 Met Val Leu Thr Asp Val Asp Leu Arg Val Lys Gln Tyr Tyr Glu Val
 130 135 140
 Pro Ile Thr Met Lys Ser Val Phe Asp Leu Ile Asp Thr Phe Gln Ser
 145 150 155 160
 Arg Ile Lys Asp Met Glu Lys Gln Lys Lys Glu Gly Ile Val Cys Lys
 165 170 175
 Glu Glu Val Gly Gly Val Leu Glu Leu Phe Pro Ile Asn Gly Ser Ser
 180 185 190
 Val Val Glu Arg Glu Asp Val Pro Ala His Leu Val Lys Asp Ile Arg
 195 200 205
 Asn Tyr Phe Gln Val Ser Pro Glu Tyr Phe Ser Met Leu Leu Val Gly
 210 215 220
 Lys Asp Gly Asn Val Lys Ser Trp Tyr Pro Ser Pro Met Trp Ser Met
 225 230 235 240
 Val Ile Val Tyr Asp Leu Ile Asp Ser Met Gln Leu Arg Arg Gln Glu
 245 250 255
 Met Ala Ile Gln Gln Ser Leu Gly Met Arg Cys Gln Lys Met Ser Met

	260		265		270										
Gln	Ala	Met	Val	Thr	Ile	Val	Thr	Thr	Lys	Asp	Thr	Arg	Met	Val	Thr
		275					280					285			
Arg	Met	Thr	Thr	Val	Ile	Met	Arg	Val	Ile	Thr	Met	Asp	Thr	Leu	Thr
	290					295					300				
Glu	Gln	Lys	Tyr	Val	Thr	Leu	Asp	Ser	Ala	Ser	Phe	Leu	Cys	Ser	Cys
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 <311> 1995-06-07
 <312> 1998-10-06

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Ile	Asn	Leu	Arg	Glu	Val	Leu	Asn	Arg	Phe	Lys	Leu	Pro	Pro	Gly	Glu
		20						25					30		
Tyr	Ile	Leu	Val	Pro	Ser	Thr	Phe	Glu	Pro	Asn	Lys	Asp	Gly	Asp	Phe
		35					40					45			
Cys	Ile	Arg	Val	Phe	Ser	Glu	Lys	Lys	Ala	Asp	Tyr	Gln	Ala	Val	Asp
	50					55					60				
Asp	Glu	Ile	Glu	Ala	Asn	Leu	Glu	Glu	Phe	Asp	Ile	Ser	Glu	Asp	Asp
	65				70					75					80
Ile	Asp	Asp	Gly	Phe	Arg	Arg	Leu	Phe	Ala	Gln	Leu	Ala	Gly	Glu	Asp
				85					90					95	
Ala	Glu	Ile	Ser	Ala	Phe	Glu	Leu	Gln	Thr	Ile	Leu	Arg	Arg	Val	Leu
			100					105					110		
Ala	Lys	Arg	Gln	Asp	Ile	Lys	Ser	Asp	Gly	Phe	Ser	Ile	Glu	Thr	Cys
		115					120					125			
Lys	Ile	Met	Val	Asp	Met	Leu	Asp	Ser	Asp	Gly	Ser	Gly	Lys	Leu	Gly
	130					135					140				
Leu	Lys	Glu	Phe	Tyr	Ile	Leu	Trp	Thr	Lys	Ile	Gln	Lys	Tyr	Gln	Lys
145					150					155					160
Ile	Tyr	Arg	Glu	Ile	Asp	Val	Asp	Arg	Ser	Gly	Thr	Met	Asn	Ser	Tyr
				165				170						175	
Glu	Met	Arg	Lys	Ala	Leu	Glu	Glu	Ala	Gly	Phe	Lys	Met	Pro	Cys	Gln
			180					185					190		
Leu	His	Gln	Val	Ile	Val	Ala	Arg	Phe	Ala	Asp	Asp	Gln	Leu	Ile	Ile
		195					200					205			
Asp	Phe	Asp	Asn	Phe	Val	Arg	Cys	Leu	Val	Arg	Leu	Glu	Thr	Leu	Phe

210	215	220
Lys Ile Phe Lys Gln Leu Asp Pro Glu Asn Thr Gly Thr Ile Glu Leu		
225	230	235 240
Asp Leu Ile Ser Trp Leu Cys Phe Ser Val Leu		
	245	250

<210> 9
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 <220>
 <223> IL-1 receptor intracellular ligand protein
 comprising amino acid sequence

 <300>
 <310> 5,817,476
 <311> 1995-06-07
 <312> 1998-10-06

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Met Ala Gly Ile Ala Ala Lys Leu Ala Lys Asp Arg Glu Ala Ala Glu
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Glu Ala Leu Arg Asn Glu Cys Leu Glu Ala Gly Thr Leu Phe Gln Asp
35 40 45
Pro Ser Phe Pro Ala Ile Pro Ser Ala Leu Gly Phe Lys Glu Leu Gly
50 55 60
Pro Tyr Ser Ser Lys Thr Arg Gly Met Arg Trp Lys Arg Pro Thr Glu
65 70 75 80
Ile Cys Ala Asp Pro Gln Phe Ile Ile Gly Gly Ala Thr Arg Thr Asp
85 90 95
Ile Cys Gln Gly Ala Leu Gly Asp Cys Trp Leu Leu Ala Ala Ile Ala
100 105 110
Ser Leu Thr Leu Asn Glu Glu Ile Leu Ala Arg Val Val Pro Leu Asn
115 120 125
Gln Ser Phe Gln Glu Asn Tyr Ala Gly Ile Phe His Phe Gln Phe Trp
130 135 140
Gln Tyr Gly Glu Trp Val Glu Val Val Val Asp Asp Arg Leu Pro Thr
145 150 155 160
Lys Asp Gly Glu Leu Leu Phe Val His Ser Ala Glu Gly Ser Glu Phe
165 170 175
Trp Ser Ala Leu Leu Glu Lys Ala Tyr Ala Lys Ile Asn Gly Cys Tyr
180 185 190
Glu Ala Leu Ser Gly Gly Ala Thr Thr Glu Gly Phe Glu Asp Phe Thr
195 200 205
Gly Gly Ile Ala Glu Trp Tyr Glu Leu Lys Lys Pro Pro Pro Asn Leu
210 215 220
Phe Lys Ile Ile Gln Lys Ala Leu Gln Lys Gly Ser Leu Leu Gly Cys

225		230		235		240
Ser Ile Asp Ile Thr	Ser Ala Ala Asp	Ser Glu Ala Ile Thr	Phe Gln			
	245		250		255	
Lys Leu Val Lys Gly His Ala Tyr	Ser Val Thr Gly Ala Glu Glu Val					
	260	265		270		
Glu Ser Asn Gly Ser Leu Gln Lys Leu Ile Arg Ile Arg	Asn Pro Trp					
	275	280	285			
Gly Glu Val Glu Trp Thr Gly Arg Trp Asn Asp	Asn Cys Pro Ser Trp					
	290	295	300			
Asn Thr Ile Asp Pro Glu Glu Arg Glu Arg	Leu Thr Arg Arg His Glu					
	305	310	315		320	
Asp Gly Glu Phe Trp Met Ser Phe Ser	Asp Phe Leu Arg His Tyr Ser					
	325	330		335		
Arg Leu Glu Ile Cys Asn Leu Thr Pro	Asp Thr Leu Thr Ser Asp Thr					
	340	345	350			
Tyr Lys Lys Trp Lys Leu Thr Lys Met Asp Gly	Asn Trp Arg Arg Gly					
	355	360	365			
Ser Thr Ala Gly Gly Cys Arg Asn Tyr Pro	Asn Thr Phe Trp Met Asn					
	370	375	380			
Pro Gln Tyr Leu Ile Lys Leu Glu Glu Glu	Asp Glu Asp Glu Glu Asp					
	385	390	395		400	
Gly Glu Ser Gly Cys Thr Phe Leu Val	Gly Leu Ile Gln Lys His Arg					
	405	410	415			
Arg Arg Gln Arg Lys Met Gly Glu Asp Met His Thr Ile	Gly Phe Gly					
	420	425	430			
Ile Tyr Glu Val Pro Glu Glu Leu Ser Gly Gln Thr	Asn Ile His Leu					
	435	440	445			
Ser Lys Asn Phe Phe Leu Thr Asn Arg Ala Arg	Glu Arg Ser Asp Thr					
	450	455	460			
Phe Ile Asn Leu Arg Glu Val Leu Asn Arg Phe Lys Leu Pro Pro	Gly					
	465	470	475		480	
Glu Tyr Ile Leu Val Pro Ser Thr Phe Glu Pro Asn Lys Asp	Gly Asp					
	485	490		495		
Phe Cys Ile Arg Val Phe Ser Glu Lys Lys Ala Asp Tyr	Gln Ala Val					
	500	505	510			
Asp Asp Glu Ile Glu Ala Asn Leu Glu Glu Phe Asp Ile Ser Glu Asp						
	515	520	525			
Asp Ile Asp Asp Gly Val Arg Arg Leu Phe Ala Gln Leu Ala Gly Glu						
	530	535	540			
Asp Ala Glu Ile Ser Ala Phe Glu Leu Gln Thr Ile Leu Arg Arg Val						
	545	550	555		560	
Leu Ala Lys Arg Gln Asp Ile Lys Ser Asp Gly Phe Ser Ile Glu Thr						
	565	570	575			
Cys Lys Ile Met Val Asp Met Leu Asp Ser Asp Gly Ser Gly Lys Leu						

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Gly	Leu	Lys	Glu	Phe	Tyr	Ile	Leu	Trp	Thr	Lys	Ile	Gln	Lys	Tyr	Gln
		595					600					605			
Lys	Ile	Tyr	Arg	Glu	Ile	Asp	Val	Asp	Arg	Ser	Gly	Thr	Met	Asn	Ser
	610					615					620				
Tyr	Glu	Met	Arg	Lys	Ala	Leu	Glu	Glu	Ala	Gly	Phe	Lys	Met	Pro	Cys
625					630					635					640
Gln	Leu	His	Gln	Val	Ile	Val	Ala	Arg	Phe	Ala	Asp	Asp	Gln	Leu	Ile
				645					650					655	
Ile	Asp	Phe	Asp	Asn	Phe	Val	Arg	Cys	Leu	Val	Arg	Leu	Glu	Thr	Leu
			660					665					670		
Phe	Lys	Ile	Phe	Lys	Gln	Leu	Asp	Pro	Glu	Asn	Thr	Gly	Thr	Ile	Glu
		675					680					685			
Leu	Asp	Leu	Ile	Ser	Trp	Leu	Cys	Phe	Ser	Val	Leu				
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<210> 10
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 <212> DNA
 <213> Artificial Sequence

<220>
 <223> Description of Artificial Sequence: Synthetic DNA
 which is antisense to human IL-1 beta

<300>
 <301> Fujiwara, Toshiyoshi
 Grimm, Elizabeth A.
 <302> Specific Inhibition of Interleukin 1 beta Gene
 Expression by an Antisense Oligonucleotide: Obligatory
 Role of Interleukin 1 in the Generation of
 Lymphokine-activated Killer Cells
 <303> Cancer Res.
 <304> 52
 <306> 4954-4959
 <307> 1992-09-15

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<210> 11
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 <212> DNA
 <213> Artificial Sequence

<220>
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 which is antisense to human IL-1 alpha

<300>
 <301> Maier, Jeanette A.
 Voulalas, Pamela
 Roeder, David
 MacLag, Thomas
 <302> Extension of the Life-Span of Human Endothelial Cells
 by an Interleukin-1 alpha Antisense Oligomer
 <303> Science
 <304> 249

<306> 1570-1574
<307> 1990-09-28

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24

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phosphorothioate DNA which is antisense to IL-1
receptor

<300>
<301> Miraglia, Loren
Geiger, Thomas
Bennett, C. Frank
Dean, Nicholas M.
<302> Inhibition of Interleukin-1 Type I Receptor Expression
in Human Cell-Lines by an Antisense Phosphorothioate
Oligodeoxynucleotide
<303> Int. J. Immunopharmacol.
<304> 18
<305> 4
<306> 227-240
<307> 1996

<400> 12
tgtgtcctgc aatcggtggc

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<210> 13
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<220>

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phosphodiester or phosphorothioate DNA which is
antisense to human IL-1 receptor

<300>
<301> Burch, Ronald M.
Mahan, Lawrence C.
<302> Oligonucleotides Antisense to the Interleukin Receptor
I mRNA Block the Effects of Interleukin I in Cultured
Murine and Human Fibroblasts and in Mice
<303> J. Clin. Invest.
<304> 88
<306> 1190-1196
<307> 1991

<400> 13
tctgagtaac actttcat

18

<210> 14
<211> 233
<212> PRT
<213> Homo sapiens

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Cachectin)

<300>

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<309> 1986-07-21

<400> 14

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Leu Ser Leu Phe Ser Phe Leu Ile Val Ala Gly Ala Thr Thr Leu Phe
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Cys Leu Leu His Phe Gly Val Ile Gly Pro Gln Arg Glu Glu Phe Pro
          50          55          60
Arg Asp Leu Ser Leu Ile Ser Pro Leu Ala Gln Ala Val Arg Ser Ser
          65          70          75          80
Ser Arg Thr Pro Ser Asp Lys Pro Val Ala His Val Val Ala Asn Pro
          85          90          95
Gln Ala Glu Gly Gln Leu Gln Trp Leu Asn Arg Arg Ala Asn Ala Leu
          100          105          110
Leu Ala Asn Gly Val Glu Leu Arg Asp Asn Gln Leu Val Val Pro Ser
          115          120          125
Glu Gly Leu Tyr Leu Ile Tyr Ser Gln Val Leu Phe Lys Gly Gln Gly
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Cys Pro Ser Thr His Val Leu Leu Thr His Thr Ile Ser Arg Ile Ala
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Val Ser Tyr Gln Thr Lys Val Asn Leu Leu Ser Ala Ile Lys Ser Pro
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Cys Gln Arg Glu Thr Pro Glu Gly Ala Glu Ala Lys Pro Trp Tyr Glu
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Pro Ile Tyr Leu Gly Gly Val Phe Gln Leu Glu Lys Gly Asp Arg Leu
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<309> 1989-03-01

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 Gln Gly Leu Pro Gly Val Gly Leu Thr Pro Ser Ala Ala Gln Thr Ala
 35 40 45
 Arg Gln His Pro Lys Met His Leu Ala His Ser Thr Leu Lys Pro Ala
 50 55 60
 Ala His Leu Ile Gly Asp Pro Ser Lys Gln Asn Ser Leu Leu Trp Arg
 65 70 75 80
 Ala Asn Thr Asp Arg Ala Phe Leu Gln Asp Gly Phe Ser Leu Ser Asn
 85 90 95
 Asn Ser Leu Leu Val Pro Thr Ser Gly Ile Tyr Phe Val Tyr Ser Gln
 100 105 110
 Val Val Phe Ser Gly Lys Ala Tyr Ser Pro Lys Ala Thr Ser Ser Pro
 115 120 125
 Leu Tyr Leu Ala His Glu Val Gln Leu Phe Ser Ser Gln Tyr Pro Phe
 130 135 140
 His Val Pro Leu Leu Ser Ser Gln Lys Met Val Tyr Pro Gly Leu Gln
 145 150 155 160
 Glu Pro Trp Leu His Ser Met Tyr His Gly Ala Ala Phe Gln Leu Thr
 165 170 175
 Gln Gly Asp Gln Leu Ser Thr His Thr Asp Gly Ile Pro His Leu Val
 180 185 190
 Leu Ser Pro Ser Thr Val Phe Phe Gly Ala Phe Ala Leu
 195 200 205

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 <309> 1993-08-03

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 35 40 45
 Tyr Ile His Pro Gln Asn Asn Ser Ile Cys Cys Thr Lys Cys His Lys
 50 55 60
 Gly Thr Tyr Leu Tyr Asn Asp Cys Pro Gly Pro Gly Gln Asp Thr Asp

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Cys Arg Glu Cys Glu Ser Gly Ser Phe Thr Ala Ser Glu Asn His Leu						
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Arg His Cys Leu Ser Cys Ser Lys Cys Arg Lys Glu Met Gly Gln Val						
	100		105		110	
Glu Ile Ser Ser Cys Thr Val Asp Arg Asp Thr Val Cys Gly Cys Arg						
	115		120		125	
Lys Asn Gln Tyr Arg His Tyr Trp Ser Glu Asn Leu Phe Gln Cys Phe						
	130		135		140	
Asn Cys Ser Leu Cys Leu Asn Gly Thr Val His Leu Ser Cys Gln Glu						
	145	150		155		160
Lys Gln Asn Thr Val Cys Thr Cys His Ala Gly Phe Phe Leu Arg Glu						
		165		170		175
Asn Glu Cys Val Ser Cys Ser Asn Cys Lys Lys Ser Leu Glu Cys Thr						
	180		185		190	
Lys Leu Cys Leu Pro Gln Ile Glu Asn Val Lys Gly Thr Glu Asp Ser						
	195		200		205	
Gly Thr Thr Val Leu Leu Pro Leu Val Ile Phe Phe Gly Leu Cys Leu						
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Leu Ser Leu Leu Phe Ile Gly Leu Met Tyr Arg Tyr Gln Arg Trp Lys						
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Ser Lys Leu Tyr Ser Ile Val Cys Gly Lys Ser Thr Pro Glu Lys Glu						
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Gly Glu Leu Glu Gly Thr Thr Thr Lys Pro Leu Ala Pro Asn Pro Ser						
	260		265		270	
Phe Ser Pro Thr Pro Gly Phe Thr Pro Thr Leu Gly Phe Ser Pro Val						
	275		280		285	
Pro Ser Ser Thr Phe Thr Ser Ser Ser Thr Tyr Thr Pro Gly Asp Cys						
	290		295		300	
Pro Asn Phe Ala Ala Pro Arg Arg Glu Val Ala Pro Pro Tyr Gln Gly						
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Ala Asp Pro Ile Leu Ala Thr Ala Leu Ala Ser Asp Pro Ile Pro Asn						
		325		330		335
Pro Leu Gln Lys Trp Glu Asp Ser Ala His Lys Pro Gln Ser Leu Asp						
		340		345		350
Thr Asp Asp Pro Ala Thr Leu Tyr Ala Val Val Glu Asn Val Pro Pro						
	355		360		365	
Leu Arg Trp Lys Glu Phe Val Arg Arg Leu Gly Leu Ser Asp His Glu						
	370		375		380	
Ile Asp Arg Leu Glu Leu Gln Asn Gly Arg Cys Leu Arg Glu Ala Gln						
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Tyr Ser Met Leu Ala Thr Trp Arg Arg Arg Thr Pro Arg Arg Glu Ala						
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Thr Leu Glu Leu Leu Gly Arg Val Leu Arg Asp Met Asp Leu Leu Gly						

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<220>
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 <309> 1991-08-01

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 35 40 45
 Thr Ala Gln Met Cys Cys Ser Lys Cys Ser Pro Gly Gln His Ala Lys
 50 55 60
 Val Phe Cys Thr Lys Thr Ser Asp Thr Val Cys Asp Ser Cys Glu Asp
 65 70 75 80
 Ser Thr Tyr Thr Gln Leu Trp Asn Trp Val Pro Glu Cys Leu Ser Cys
 85 90 95
 Gly Ser Arg Cys Ser Ser Asp Gln Val Glu Thr Gln Ala Cys Thr Arg
 100 105 110
 Glu Gln Asn Arg Ile Cys Thr Cys Arg Pro Gly Trp Tyr Cys Ala Leu
 115 120 125
 Ser Lys Gln Glu Gly Cys Arg Leu Cys Ala Pro Leu Arg Lys Cys Arg
 130 135 140
 Pro Gly Phe Gly Val Ala Arg Pro Gly Thr Glu Thr Ser Asp Val Val
 145 150 155 160
 Cys Lys Pro Cys Ala Pro Gly Thr Phe Ser Asn Thr Thr Ser Ser Thr
 165 170 175
 Asp Ile Cys Arg Pro His Gln Ile Cys Asn Val Val Ala Ile Pro Gly
 180 185 190
 Asn Ala Ser Arg Asp Ala Val Cys Thr Ser Thr Ser Pro Thr Arg Ser
 195 200 205
 Met Ala Pro Gly Ala Val His Leu Pro Gln Pro Val Ser Thr Arg Ser
 210 215 220

Gln His Thr Gln Pro Thr Pro Glu Pro Ser Thr Ala Pro Ser Thr Ser
 225 230 235 240
 Phe Leu Leu Pro Met Gly Pro Ser Pro Pro Ala Glu Gly Ser Thr Gly
 245 250 255
 Asp Phe Ala Leu Pro Val Gly Leu Ile Val Gly Val Thr Ala Leu Gly
 260 265 270
 Leu Leu Ile Ile Gly Val Val Asn Cys Val Ile Met Thr Gln Val Lys
 275 280 285
 Lys Lys Pro Leu Cys Leu Gln Arg Glu Ala Lys Val Pro His Leu Pro
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 Ala Asp Lys Ala Arg Gly Thr Gln Gly Pro Glu Gln Gln His Leu Leu
 305 310 315 320
 Ile Thr Ala Pro Ser Ser Ser Ser Ser Ser Leu Glu Ser Ser Ala Ser
 325 330 335
 Ala Leu Asp Arg Arg Ala Pro Thr Arg Asn Gln Pro Gln Ala Pro Gly
 340 345 350
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 355 360 365
 Asp Ser Ser Pro Gly Gly His Gly Thr Gln Val Asn Val Thr Cys Ile
 370 375 380
 Val Asn Val Cys Ser Ser Ser Asp His Ser Ser Gln Cys Ser Ser Gln
 385 390 395 400
 Ala Ser Ser Thr Met Gly Asp Thr Asp Ser Ser Pro Ser Glu Ser Pro
 405 410 415
 Lys Asp Glu Gln Val Pro Phe Ser Lys Glu Glu Cys Ala Phe Arg Ser
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 <311> 1995-06-19
 <312> 1998-12-15

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Arg	Val	Tyr	Leu	Tyr	Glu	Gly	Leu	Leu	Gly	Lys	Glu	Arg	Ser	Thr	Leu
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Leu	Glu	Arg	Glu	Gly	Met	Gly	Met	Asp	Gln	Gly	Pro	Gln	Glu	Met	Ile
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Asp	Arg	Tyr	Leu	Ser	Leu	Gly	Glu	His	Asp	Arg	Lys	Arg	Leu	Glu	Asp
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Arg	Leu	Met	Gly	Lys	Ser	His	Ile	Gly	Leu	Val	Tyr	Ser	Gln	Gln	Ile
				165					170					175	
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			180					185					190		
Ile	Trp	Ser	Ser	Gly	Ser	Arg	His	Met	Lys	Lys	Gln	Thr	Phe	Val	Val
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Asp	Asp	Cys	Val	Val	Leu	Arg	Ser	Asn	Ile	Gly	Thr	Val	Tyr	Glu	Arg
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Trp	Trp	Tyr	Glu	Lys	Leu	Ile	Asn	Met	Thr	Tyr	Cys	Pro	Lys	Thr	Lys
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Val	Leu	Cys	Leu	Trp	Arg	Arg	Asn	Gly	Ser	Glu	Thr	Gln	Leu	Asn	Lys
			260					265					270		
Phe	Tyr	Thr	Lys	Lys	Cys	Arg	Glu	Leu	Tyr	Tyr	Cys	Val	Lys	Asp	Ser
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Leu	Gly	Gly	Glu	Phe	Pro	Val	Gln	Asp	Leu	Lys	Thr	Gly	Glu	Gly	Gly
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Leu	Leu	Gln	Val	Thr	Leu	Glu	Gly	Ile	Asn	Leu	Lys	Phe	Met	His	Asn
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Gln	Val	Phe	Ile	Glu	Leu	Asn	His	Ile	Lys	Lys	Cys	Asn	Thr	Val	Arg
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Gly	Val	Phe	Val	Leu	Glu	Glu	Phe	Val	Pro	Glu	Ile	Lys	Glu	Val	Val
		355					360					365			
Ser	His	Lys	Tyr	Lys	Thr	Pro	Met	Ala	His	Glu	Ile	Cys	Tyr	Ser	Val

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 comprising amino acid sequence

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 <311> 1995-06-19
 <312> 1998-12-15

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 35 40 45
 Arg Ile Pro Gln Val Thr Thr His Trp Leu Glu Ile Leu Gln Ala Leu
 50 55 60
 Leu Leu Ser Ser Asn Gln Glu Leu Gln His Arg Gly Ala Val Val Val
 65 70 75 80
 Leu Asn Met Val Glu Ala Ser Arg Glu Ile Ala Ser Thr Leu Met Glu
 85 90 95
 Ser Glu Met Met Glu Ile Leu Ser Val Leu Ala Lys Gly Asp His Ser
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 Pro Val Thr Arg Ala Ala Ala Ala Cys Leu Asp Lys Ala Val Glu Tyr
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35 40 45
Ala Arg Ala Val Glu Ser Phe Leu Arg Gly Thr Thr Ser Tyr Ala Asp
50 55 60
Gln Met Phe Leu Leu Lys Arg Gly Leu Leu Glu His Ile Leu Tyr Cys
65 70 75 80
Ile Val Asp Ser Glu Cys Lys Ser Arg Asp Val Leu Gln Ser Tyr Phe
85 90 95
Asp Leu Leu Gly Glu Leu Met Lys Phe Asn Val Asp Ala Phe Lys Arg
100 105 110
Phe Asn Lys Tyr Ile Asn Thr Asp Ala Lys Phe Gln Val Phe Leu Lys
115 120 125
Gln Ile Asn Ser Ser Leu Val Asp Ser Asn Met Leu Val Arg Cys Val
130 135 140
Thr Leu Ser Leu Asp Arg Phe Glu Asn Gln Val Asp Met Lys Val Ala
145 150 155 160
Glu Val Leu Ser Glu Cys Arg Leu Leu Ala Tyr Ile Ser Gln Val Pro
165 170 175
Thr Gln Met Ser Phe Leu Phe Arg Leu Ile Asn Ile Ile His Val Gln
180 185 190
Thr Leu Thr Gln Glu Asn Val Ser Cys Leu Asn Thr Ser Leu Val Ile
195 200 205
Leu Met Leu Ala Arg Arg Lys Glu Arg Leu Pro Leu Tyr Leu Arg Leu
210 215 220
Leu Gln Arg Met Glu His Ser Lys Lys Tyr Pro Gly Phe Leu Leu Asn
225 230 235 240

Asn Phe His Asn Leu Leu Arg Phe Trp Gln Gln His Tyr Leu His Lys
245 250 255
Asp Lys Asp Ser Thr Cys Leu Glu Asn Ser Ser Cys Ile Ser Phe Ser
260 265 270
Tyr Trp Lys Glu Thr Val Ser Ile Leu Leu Asn Pro Asp Arg Gln Ser
275 280 285
Pro Ser Ala Leu Val Ser Tyr Ile Glu Glu Pro Tyr Met Asp Ile Asp
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Arg Asp Phe Thr Glu Glu
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 comprising amino acid sequence

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 35 40 45
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 50 55 60
 Thr Pro Val Gly Lys Asp Pro Gly Leu Ala Gly Arg Gly Asp Pro Lys
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 Ala Met Ala Gln Leu Arg Val Pro Gln Leu Gly Pro Arg Ala Pro Ser
 85 90 95
 Ala Thr Gly Lys Gly Pro Lys Glu Leu Asp Thr Arg Ser Leu Lys Glu
 100 105 110
 Glu Asn Phe Ile Ala Ser Ile Gly Pro Glu Val Ile Lys Pro Val Phe
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 Asp Leu Gly Glu Thr Glu Glu Lys Lys Ser Gln Ile Ser Ala Asp Ser
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 Gly Val Ser Leu Thr Ser Ser Ser Gln Arg Thr Asp Gln Asp Ser Val
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 165 170 175
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 180 185 190
 Asp Ser Asp Leu Ser Ser Asn Ala Gly Asp Gly Pro Gly Gly Glu Gly
 195 200 205
 Ser Val His Leu Ala Ser Ser Arg Gly Thr Leu Ser Asp Ser Glu Ile
 210 215 220
 Glu Thr Asn Ser Ala Thr Ser Thr Ile Phe Gly Lys Ala His Ser Leu
 225 230 235 240
 Lys Pro Ser Ile Lys Glu Lys Leu Ala Gly Ser Pro Ile Arg Thr Ser
 245 250 255
 Glu Asp Val Ser Gln Arg Val Tyr Leu Tyr Glu Gly Leu Leu Gly Lys
 260 265 270
 Glu Arg Ser Thr Leu Trp Asp Gln Met Gln Phe Trp Glu Asp Ala Phe

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Pro	Gln	Glu	Met	Ile	Asp	Arg	Tyr	Leu	Ser	Leu	Gly	Glu	His	Asp	Arg
305					310					315					320
Lys	Arg	Leu	Glu	Asp	Asp	Glu	Asp	Arg	Leu	Leu	Ala	Thr	Leu	Leu	His
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Asn	Leu	Ile	Ser	Tyr	Met	Leu	Leu	Met	Lys	Val	Asn	Lys	Asn	Asp	Ile
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Arg	Lys	Lys	Val	Arg	Arg	Leu	Met	Gly	Lys	Ser	His	Ile	Gly	Leu	Val
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Tyr	Ser	Gln	Gln	Ile	Asn	Glu	Val	Leu	Asp	Gln	Leu	Ala	Asn	Leu	Asn
						375					380				
Gly	Arg	Asp	Leu	Ser	Ile	Trp	Ser	Ser	Gly	Ser	Arg	His	Met	Lys	Lys
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Gln	Thr	Phe	Val	Val	His	Ala	Gly	Thr	Asp	Thr	Asn	Gly	Asp	Ile	Phe
				405					410					415	
Phe	Met	Glu	Val	Cys	Asp	Asp	Cys	Val	Val	Leu	Arg	Ser	Asn	Ile	Gly
			420					425					430		
Thr	Val	Tyr	Glu	Arg	Trp	Trp	Tyr	Glu	Lys	Leu	Ile	Asn	Met	Thr	Tyr
		435					440					445			
Cys	Pro	Lys	Thr	Lys	Val	Leu	Cys	Leu	Trp	Arg	Arg	Asn	Gly	Ser	Glu
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Thr	Gln	Leu	Asn	Lys	Phe	Tyr	Thr	Lys	Lys	Cys	Arg	Glu	Leu	Tyr	Tyr
465					470					475					480
Cys	Val	Lys	Asp	Ser	Met	Glu	Arg	Ala	Ala	Ala	Arg	Gln	Gln	Ser	Ile
				485					490					495	
Lys	Pro	Gly	Pro	Glu	Leu	Gly	Gly	Glu	Phe	Pro	Val	Gln	Asp	Leu	Lys
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Thr	Gly	Glu	Gly	Gly	Leu	Leu	Gln	Val	Thr	Leu	Glu	Gly	Ile	Asn	Leu
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Lys	Phe	Met	His	Asn	Gln	Val	Phe	Ile	Glu	Leu	Asn	His	Ile	Lys	Lys
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Ile	Lys	Glu	Val	Val	Ser	His	Lys	Tyr	Lys	Thr	Pro	Met	Ala	His	Glu
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Ile	Cys	Tyr	Ser	Val	Leu	Cys	Leu	Phe	Ser	Tyr	Val	Ala	Ala	Val	His
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 which is antisense to TNF-alpha
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 <310> 5,705,389
 <311> 1994-11-18
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 upper primer for Dengue virus type 2 detection
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 lower primer for Dengue virus type 2 detection
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 <210> 25
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 lower primer for IL-1ra detection
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